PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference AHBCP6281273	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/GB2005/000459	International filing date *(day/month/year)* 11 February 2005 (11.02.2005)	Priority date *(day/month/year)* 11 February 2004 (11.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THE UNIVERSITY OF YORK		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 14 August 2006 (14.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Nora Lindner e-mail: pt02@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/000459	11.02.2005	11.02.2004

International Patent Classification (IPC) or both national classification and IPC
C12N15/11, A61K38/00, G01N33/50

Applicant
THE UNIVERSITY OF YORK

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Durrenberger, A Telephone No. +49 89 2399-8432

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000459

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-3, 22

because:

☒ the said international application, or the said claims Nos. 1-3, 22 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3, 13, 16-23
	No:	Claims	1,2,4-12,14,15, 24-26
Inventive step (IS)	Yes:	Claims	20
	No:	Claims	1-19, 21-26
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	see separate sheet

2. Citations and explanations

see separate sheet

Concerning section III

Claims 1-3, 22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Concerning section V

1. The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

   D1: US 2003/124101 A1 (GU WEI ET AL) 3 July 2003 (2003-07-03)
   D2: WO 01/51051 A (HAREL, AVIKAM; BLOCH, OLGA) 19 July 2001 (2001-07-19)

   Unless indicated otherwise reference is made to the relevant passages emphasized in the search report.

2. The document D1 discloses the use of SIRT1 (human SIR2α) inhibitors (nicotinamide, Vitamin B3, SIRT1 antisense, ribozymes, DNAzymes) to inhibit p53 inhibition in vitro and in vivo, thereby inducing apoptosis and treating cancer. Hence D1 anticipates the subject-matter of claims 1, 2, 4-12, 14, 15.

   D1 further discloses the identification of nicotinamide as SIRT1 inhibitor by administering nicotinamide to cells and testing SIRT1 expression/activity and apoptosis (see paragraphs [0072] to [0080], thereby anticipating the subject-matter of claims 24-26.

   The document D2 discloses the use of the SIRT1 inhibitor nicotinamide to treat proliferative disorders like cancer and psoriasis, thereby anticipating the subject-matter of claims 1, 2, 8, 9, 11, 12.

3. The closest prior art is the document D1 which discloses that inhibition of SIRT1 by

e.g. nicotinamide induces apoptosis *via* p53. Inhibitors of SIRT1 are therefore useful for the treatment of cancer.
The application differs from D1 by the use of siRNA, or the treatment of colorectal carcinoma specifically.
The problem of the invention is to provide an alternative treatment of cancer.
The solution is the use of SIRT1 siRNA, in particular for the treatment of colorectal cancer.

The protein SIRT1 is known in the art, as well as the use of anti-SIRT1 nucleic acids as inhibitors. The technique of siRNA is a well-known alternative among inhibiting nucleic acids like antisense. In view of the teaching of D1 to use SIRT1 inhibiting nucleic acids, the skilled person does not need inventive skills to manufacture SIRT1 siRNAs in general. Hence the subject-matter of claims 16 to 19 and 21 to 23, relating to any SIRT1 siRNA is not inventive. Furthermore, not any sequence of 19 to 22 bp is expected to efficiently inhibit SIRT1, hence, as these claims have not been shown to work on the whole claimed range, they are not inventive.
Only the subject-matter of claim 20 relating to particular, defined and tested SIRT1 siRNAs can be acknowledged as inventive as the skilled person is given no hint to try these particular sequences.

Concerning the treatment of colorectal carcinoma over cancer in general as disclosed in D1, the skilled person would expect inhibitors of SIRT1 to be useful for any type of cancer, hence the subject-matter of claims 3 and 13 is not inventive.

4. For the assessment of the present claims 1-3, 22 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.